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Is the prevalence of arterial hypertension in rheumatoid arthritis and osteoarthritis associated with disease?

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Short title:
Hypertension in RA and OA

Abstract

Objective. In this study, we compare the prevalence of HT in RA and OA patients, exposed to high- and low-grade chronic inflammation, respectively , to assess the possible association between chronic inflammation and HT.

Methods. A total of consecutive 627 RA and 352 OA patients were enrolled in this multicentric study. HT was defined as a systolic blood pressure (BP) ≥140 and/or diastolic BP ≥90 mmHg or current use of any antihypertensive drug. Overweight/obesity was defined as body mass index (BMI) ≥25, and patients ≥65 years old were considered elderly.

Results. The prevalence of HT was higher in the OA group than in the RA group [73.3% (95%CI 68.4, 77.7) and 59.5% (95%CI 55.6, 68.4) P<0.001 respectively]. When the results were adjusted for age and BMI the HT prevalence was similar in both groups [RA 59%(95%CI 55.1, 63.8) OA 60%(95%CI 58.4, 65.0)]. In both groups, the prevalence of HT was higher in the elderly and those who were overweight than in the younger patients and those with a BMI <25 . Overweight (BMI ≥25) and age ≥65 were independent predictors of HT in multivariate logistic regression model, which show no association of HT and the disease (RA or OA).

Conclusion. The results indicated a robust association of age and BMI with HT prevalence in both RA and OA. The difference in HT prevalence between RA and OA is rather due to age and BMI then to features of the disease, putting into question specific association of HT with RA.

Key words: Rheumatoid arthritis, Osteoarthritis, Hypertension

Introduction

Excessive cardiovascular (CV) morbidity and mortality leading to premature death is common in rheumatoid arthritis (RA) patients. The mechanism of this co-morbidity is not well understood. Chronic systemic inflammation is thought to have a pivotal role in increased CV disease risk in RA, contributing to vascular damage (endothelial dysfunction, accelerated atherosclerosis, and atherosclerotic plaque instability) [1].

Among the classic CV risk factors, hypertension (HT) has a prominent role in RA patients [1,2]. An increased prevalence of HT in RA patients was found in a number of studies, but not in all. A 52-73% prevalence of HT in RA patients was found in the studies with a large number of patients that used the current definition of hypertension [3]. The mechanisms leading to frequent HT in RA patients are not clear; the association is likely due to a complex interplay of various factors, including chronic systemic inflammation [3].

CV co-morbidities, particularly HT, have not been investigated in osteoarthritis (OA) patients as extensively as in RA patients. The prevalence of CV disease in OA was found to be approximately 55% [4,5]. The reported prevalence of HT in OA was 40% in one study [6] and 75% in another [7]. The studies comparing CV disease risk in RA and OA are rather scarce. The CV disease risk and the presence of CV disease risk factors in OA were found to be lower [8] or similar [9] to those in RA. The CV disease risk in OA has been attributed to a high prevalence of classic CV disease risk [9], and in the case of HT, to medication, especially the use of non-steroidal anti-inflammatory drugs (NSAIDs) and cyclooxygenase-2 inhibitors [10].

The aim of this study is a comparison of HT prevalence and disease features in RA and OA patients. A comparison of the two diseases, which are both characterized by a chronic course and painful joint involvement, but with either high (RA) or low (OA) levels of chronic systemic inflammation [11,12], may reveal an association between various disease features and HT in conditions that differ in terms of the level of chronic systemic inflammation.

Patients and methods

In order to collect date concerning HT prevalence in RA and OA of from all part of the country we preformed this multicentric cross-sectional study in collaboration with outpatient rheumatology clinics in regional medical centers of Croatia (Table 1). A total of 625 RA and 352 OA patients who attended the outpatient clinics from 1 September to 31 December 2009 were consecutively enrolled in the study. The diagnoses of RA and OA (knee, hip and hand) were established by qualified rheumatologists according to the 1987 American College of Rheumatology

(ACR) classification criteria for RA [13] and the ACR criteria for OA [14,15,16]. The study protocol was approved by the Ethical Committee of the Dubrava University Hospital, Zagreb, the coordinative center of the study, and a written informed consent (according to the Declaration of Helsinki) was obtained from all study participants.

All participants underwent a detailed evaluation guided by a questionnaire administered in all collaborative departments. The evaluation included a detailed medical history, physical examination and the measurement of body height and weight. Patients with ischemic heart disease were not included in the study.

In order to compare this study with the study [17] the subgroups comprised all 50-70 yrs old RA and OA patients were selected.

Patients ≥65 years of age were considered elderly. Body mass index (BMI) was calculated according to the standard formula [18], and patients with BMIs ≥25 were qualified as overweight (including obesity). Waist and hip circumferences were measured, and the waist-to-hip ratio (WHR) was calculated [19].

Pain and the patients' general health (GH) were assessed using the appropriate visual analog scales (VAS). Pain VAS (VASP) ranged from 0–10, with 10 being the most intensive pain [20]. General health VAS (VASGH) was part of the DAS28-CRP score [21]. VAS was represented by a 100 mm long line on which the patients evaluated their own health, with 100 mm representing the best health. RA patient functional status and disease activity were assessed by the Croatian translation of the Health Assessment Questionnaire (HAQ)[22] and by the DAS28-CRP [20] using a DAS calculator [23], respectively.

All antihypertensive and antirheumatic medications taken by the enrolled patients were recorded in detail (indications, dose and duration of treatment).

Blood pressure (BP) was measured after a 5 min rest in a sitting position on the right arm with a mercury sphygmomanometer and a standard cuff. The recorded BP value for each patient was the mean of three subsequent measurements at 5 min intervals. HA was defined according to the European Society of Hypertension and the European Society of Cardiology 2007 guidelines with BP≥140 mmHg and/or diastolic BP≥90 mmHg [18] or any BP with antihypertensive treatment. Newly discovered HT was defined as actual HT without HT history and was expressed as the prevalence and the fraction of actual HT. Uncontrolled HT was defined as HT on hypertensive therapy having BP with HT values.

Venous blood samples were collected for laboratory investigations after overnight fasting. The following tests were performed in the laboratories of the collaborative hospitals: erythrocyte

sedimentation rate (ESR), C-reactive protein (CRP), total cholesterol (Chol), high-density lipoproteins (HDL), low-density lipoproteins (LDL), triglycerides (TG), creatinine and plasma glucose (Glc). When required, oral glucose tolerant tests (OGTT) were performed. Diabetes (DM) was defined by a history of DM with current use of antidiabetic medication or fasting Glc ≥7 mmol/L or Glc in OGTT (2 h) ≥11.1 mmol/L [24]. The same standard methods were used in all laboratories, and biochemical assays were performed using Olympus autoanalyzers according to the manufacturer's protocol.

Statistical analysis

The normality of the data distribution was assessed using the Kolgomorov-Smirnov test. Values are presented as median [interquartile range(IQR], mean (S.D.) or percentage values as appropriate. Comparisons were performed with the Student's t-test, Mann-Whitney U-test and chi-squared test for normally, non-normally distributed and categorical variables, respectively. Binary logistic regression was used to assess the independency of the association of various variables with the prevalence of HT in RA, OA and all patients. P-values <0.05 (two-tailed) were considered significant. All statistical analyses were performed using SPSS 17.0 software (SPSS Inc., Chicago, USA). The adjustment of HT prevalence for age and BMI was made according to [25].

Results

Characteristics of RA and OA patients (Table 2).

The proportion of female patients was higher than that of men in both the RA and OA groups. In comparison with OA, RA was characterized by younger age, a lower proportion of elderly patients, a longer duration of the disease, a higher proportion of smokers (ever and current), lower BMI and WHR, a lower proportion of overweight/obese patients, similar VASP and VASGH, and lower proportions of dyslipidemic and DM patients.

Laboratory investigations showed higher plasma CRP concentrations and ESR, and lower Chol, TC and Glc plasma concentrations in the RA group. HDL, LDL and plasma creatinine concentrations were similar in both groups of patients.

Prevalence of HT in RA and OA patients (Table 3)

The prevalence of HT was lower in the RA group than in the OA group. However when the results were adjusted for age and BMI the prevalence was similar in both groups. Also HT prevalence in RA and OA of 55-70 yrs subgroups was similar.

The proportion of patients with a history of HT was lower the RA group than in the OA group. The prevalence of newly discovered HT was similar in RA and OA, but newly discovered

HT comprised a higher fraction of actual HT in RA than in OA patients. The rate of uncontrolled HT, expressed as fraction of treated HT was similar in the RA and OA groups.

In both RA and OA, the prevalence of HT was higher in the elderly and overweight/obese patients than in patients under 65 years of age or with BMI values <25. When RA and OA patients less than 65 years of age were sorted according to both age and BMI, the prevalence of HT was higher in overweight/obese patients than in those with BMI values <25. In the elderly, this difference was smaller and statistically insignificant.

Taking cut-off for CRP concentration of 5 mg/L, the prevalence of HT was higher in the RA group with higher CRP concentration then with lower. In the OA there was no such difference.

In both RA and OA patients, the prevalence of HT was higher in DM than in nondiabetic patients. Upon comparing RA and OA, the prevalence of HT in DM was similar in both groups and that in nondiabetics was higher in the latter group than in the former group.

Regarding smoking habit, HT prevalence was higher in non-smoker and ex-smokers then in current smokers in both groups.

The HT prevalence was similar in non-steroidal anti-inflammatory drugs (NSAIDs) users and non-users in both the RA and OA groups. In RA group there was no difference in HT prevalence between glucocorticoid users and non-users, but in current users the prevalence of HT was higher in patients taking glucocorticoids more then less of 3 months.

Results regarding comparison of HT and NT (normotensive) subgroups of RA and OA patients and comparison of hypertensive RA and OA patients are shown in table 1-S and 2-S. (see supplementary data available at *Rheumatology* online)

Multivariate analysis

Variables that were significantly different comparing the HT and NT subgroups in RA and OA groups were introduced in logistic regression the models. The variables that were independently associated with HT presence in RA and OA were age and BMI (see see supplementary data available at *Rheumatology* online table 2-S). To analyze mutual contribution of these variables to HT prevalence in all patents in a logistic regression model age and BMI as numerical variables and the disease (RA or OA) as categorical variable were introduced (table 4). The analysis indicated independent association of age and BMI with HT prevalence without contribution of features of the disease (RA or OA). From the date generated by the model adjusted HT prevalence were calculated (table 3).

Discussion

The characteristics of our RA and OA patients and their differences are consistent with reported epidemiological and clinical features of the diseases [26], including a higher prevalence in females than in males in both RA and OA; higher age in OA and a longer duration of the disease for RA, higher proportion of smokers in RA, reflect a greater increase in OA prevalence with age and a lower age of onset of RA; and a strong association of BMI with OA and an association of RA with smoking.

The prevalence of HT is associated with age [27] and BMI [28], which explains the higher prevalence of HT in OA. When the results were adjusted for age and BMI the HT prevalence in RA and OA was similar.

In comparison with others studies, the prevalence of HT in RA group was lower than that reported in a similar study of Panoulas et al. [17], The patients in that study was older then in this study [63.1(55-69.6) v 59.00(52.00-68.00) median (IQR) respectively]. Similar HT prevalence in 55-70 yrs RA subgroups and that in [17] study indicate that the differences in HT prevalence between this study and study [17] is due to difference in age of the patients. Regarding OA, our finding is similar to that reported in one of the previous studies [7].

The overall prevalence of HT in Croatia (44.2%) is similar to that in other European countries [29].When age was taken into account, only the higher prevalence of HT in OA patients under 65 years old, compared with the prevalence in the general Croatian population, could be assumed (Fig. 1). However, this visual comparison of prevalence and the confidence intervals is rather insufficient, and investigations with proper control groups are needed.

Upon comparing the rates of newly discovered, treated with antihypertensive therapy and uncontrolled HT in our study with rates in the general Croatian population [29] and rates described for RA [28], there was a lower rate for newly discovered HT (reference 29: 44.5%; reference 28: 39.4% vs. this study: 29.9% and 18.6% for RA and OA, respectively), a higher rate for treated HT (reference 29: 44.5%; reference 28: 60.6% vs. this study: 75.1% and 86.0% for RA and OA, respectively) and a lower rate for uncontrolled HT (reference 29: 85.6%; reference 28: 78.36% vs. this study: 41.0% and 50.8% for RA and OA, respectively). This improvement in HT screening and therapy in rheumatologic diseases is probably result of recently increased awareness of HT prevalence in RA [17,30]

In both RA and OA, the association of HT with various variables followed that of HT in general (increased HT prevalence with age and BMI, association of HT with DM and with metabolic variables associated with HT, (see supplementary data available at *Rheumatology* online table 1-S)[18] and were similar to those described for RA [17].

Due to the change in body composition (loss of lean body mass with an increase in fat body mass) in RA, BMI is lower for a given fat mass [31], which should be taken in account when BMI in RA is compared with that in other conditions. Alternatively, we measured WHR, which correlates with visceral adipose tissue and CV disease risk [19]. The higher WHR in OA (all patients) indicates a higher visceral adiposity in OA than in RA. Lower BMI values and similar WHRs in HT RA versus HT OA patients may indicate an underestimation of overweight and obesity in the former group (see Supplementary data table 1-S).

The prevalence of HT in subgroups defined by both age and BMI (higher in the subgroup with BMI≥25 than BMI<25 in patients <65 years of age and similar regarding BMI in patients ≥65 years of age) indicated a stronger association between age and HT than between BMI and HT.

Smoking has been shown to be a risk factor for HT in general [18], and an association with HT in RA has been described [17]. The lack of association of smoking with HT in both RA and OA in our study might be explained by the higher age of nonsmokers versus current smokers and ex-smokers in both the RA and OA groups (results not shown).

Higher values for markers of inflammation (ESR, CRP concentration) in RA compared to OA, as well as in the RA HT subgroup compared to NT RA (see supplementary data available at *Rheumatology* online 1-S) and higher HT prevalence in CRP>5mg/L than in CRP<5mg/L RA subgroup, show a higher grade of systemic inflammation in RA than in OA and an association of HT with degree of systemic inflammation in RA, respectively. This association was rather weak because it was not expressed in the multivariate analysis (see supplementary data available at *Rheumatology* online table 2-S), and there was no association of disease activity and HT assessed by the DAS28-CRP (see supplementary data available at *Rheumatology* online table 1). In a retrospective study, an association between CRP concentration and HT was shown in RA [2], whereas no association of HT with either CRP or DAS was found in the cross-sectional study [17]. A causative role of systemic inflammation in the pathogenesis of HT in RA was proposed, but there was no conclusive evidence for that hypothesis [3,17]. Cross-sectional studies with one point of measurement for inflammatory markers and HT, such as this study and that reported in [17], are not adequate to answer questions regarding the duration of disease, and future longitudinal studies are essential.

Antirheumatic therapy may provoke HT or interfere with its control, particularly in the case of NSAIDs used for the treatment of OA [10] and RA and for various DMARDs and GCs used to treat RA [3]. Our results, which showed no association of HT with NSAID use in RA and OA and an association of HT with leflunomide use (see supplementary data available at *Rheumatology*

online, table 1-S) and with the duration of GC use in RA were similar to the findings of others for RA [17,32].

Finally, age and BMI were the only variables that were independently associated with HT in both the RA and OA groups and with difference in HT presence between RA and OA. However, age and BMI, which are higher in OA than in RA, act as confounding variables that may obscure the association of other variables with HT, particularly systemic inflammation [33], and the influence of these variables could not be excluded.

Confounding effect of age and BMI has to be taken in account in comparison of HT prevalence between RA and OA and with other conditions to avoid erroneously conclusions.

In conclusion, this cross-sectional study has shown a robust association of age and BMI with HT prevalence in both RA and OA. The difference in HT prevalence between RA and OA is rather due to age and BMI than due to features of the disease, putting into question specific association of HT and RA [3].

Indirect comparison showed that HT prevalence in RA in our study was similar to the Croatian general population. For OA, HT prevalence was higher than that of the Croatian general population under 65 years old and similar to that over 65 years old.

Key messege

The difference in HT prevalence between RA and OA is due to age and BMI.

Confounding effect of age and BMI could lead to erroneously conclusions on HT prevalence.

HT prevalence in RA is similar to that in general population in Croatia.

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Disclosure statement

The authors declare no conflicts of interest.

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Online Resource

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Table 1-S. Hypertensive and normotensive patients in RA[a] and OA[b]

	RA (N=627)			P value (HTRA vs. HTOA)	OA (N=352)		
	HT[c] (N=373)	NT[d] (N=254)	P-value(HT vs. NT)		HT (N=258)	NT (N=94)	P-value (HT vs. NT)
Sex female, n[%(95%CI[e])]	314 [84.2 (80.2, 87.6)]	208 [81.0 (75.7, 85.3)]	0.450	0.435	223 [86.4 (81.7, 90.0)]	72 [76.6 (67.1, 84.0)]	0.027
Age, yrs	63.0 (56.0-70.0)	54.0 (45.0-62.0)	<0.001	<0.001	69.0 (61.0-74.0)	59.0 (50.0-69.0)	<0.001
Aged ≥65 yrs, n[%(95%CI)]	157 [42.1 (37.2, 47.2)]	51 [20.1 (15.6, 25.5)]	<0.001	<0.001	167 [64.7 (58.7, 70.3)]	32 [34.0 (25.2, 44.0)]	<0.001
Disease duration (yrs)	8.0 (3.0 -16.0)	5.0 (2.0 -12.0)	0.002	0.008	6.00 (2.0-12.0)	3.0 (1.0-7.0)	<0.001
HT awareness (yrs)	7.0 (3.0-13.0)	0	ND[g]	0.002	9.0 (5.0-16.0)	0	ND
BMI[f]	27.17 (24.66 - 30.26)	25.30 (22.58 -28.03)	<0.001	<0.001	30.41 (26.73 -33.00)	27.50 (24.96 - 31.03)	<0.001
BMI≥ 25 n[%(95%CI)]	266 [71.3 (66.5, 75.7)]	129 [50.7 (44.6, 56.8)]	<0.001	<0.001	218 [85.2 (80.4, 89.0)]	70 [74.5 (64.8, 82.2)]	0.020
W/H[h] ratio	0.90 (0.85 - 0.95)	0.86 (0.80 - 0.92)	<0.001	0.464	0.90 (0.85 - 0.96)	0.89 (0.82 - 0.96)	0.177
VASP[i]	50.00 (39.00 - 70.00)	50.00 (25.25 - 70.00)	0.007	0.340	55.00 (40.00 - 70.00)	40.00 (28.00 - 50.00)	<0.001
VASGH[j]	50.00 (30.00 - 70.00)	42.00 (20.00 - 60.00)	0.064	0.618	50.00 (30.00 - 64.50)	43.50 (30.00 - 60.00)	0.147
HAQ[k]	1.50 (0.70 - 2.13)	1.19 (0.60 - 1.88)	0.002		ND	ND	ND
DAS28-CRP[l]	4.41 (1.52)	4.21 (1.58)	0.129		ND	ND	
Dyslipidemia, n[%(95%CI)]	173 [46.4 (41.4, 51.5)]	76 [29.9 (24.6, 35.8)]	<0.001	0.030	147 [57.0 (50.9, 62.9)]	37 [39.4 (30.1, 49.5)]	0.010
DM[m] n[%(95%CI)]	47 [12.6 (9.6, 16.4)]	13 [5.1 (3.0, 8.5)]	0.002	0.010	52 [20.2 (15.8, 25.5)]	7 [7.4 (3.6, 14.5)]	0.005
Laboratory data							
ESR[n]	28 (15 – 45)	22 (12 – 40)	0.007	<0.001	15 (9- 24)	12 (8 – 20)	0.114
CRP[o] (mg/L)	9.40 (4.00-21.00)	6.70 (2.38-16.94)	0.007	<0.001	2.95 (1.30-3.83)	2.00 (1.40 – 3.10)	0.016
Chol[p] (mmol/L)	5.61 (4.90 – 6.50)	5.30 (4.73 – 5.90)	<0.001	0.565	5.80 (4.84 – 6.60)	5.70 (4.80 – 6.38)	0.263
TG[q] (mmol/L)	1.45 (1.10 – 1.90)	1.22 (0.93 – 1.60)	<0.001	<0.001	1.700 (1.30 – 2.31)	1.60 (1.09 – 1.90)	0.008

HDL[r] (mmol/L)	1.40 (1.19 – 1.80)	1.43 (1.20 – 1.79)	0.403	0.920	1.40 (1.19 – 1.70)	1.50 (1.20 – 1.80)	0.073
LDL[s] (mmol/L)	3.40 (2.90 – 4.05)	3.12 (2.70 – 3.70)	<0.001	0.038	3.23 (2.50 – 3.969	3.01 (2.30 – 3.73)	0.100
Glc[t] (mmol/L)	5.00 (4.50 – 5.60)	4.90 (4.40 – 5.30)	0.007	<0.001	5.50 (4.90 – 6.00)	5.40 (5.00 – 5.89)	0.350
Creatinine (mmol/L)	78.00 (69.00 – 88.75)	74.00 (65.00 – 82.25)	<0.001	0.768	79.00 (68.00 – 89.00)	78.00 (70.00 – 84.25)	0.629
RF[u] (IU/mL)	46.3 (10.0-155.0)	28.8 (8.0-139.5)	0,268	ND	ND	ND	ND
Smoking habit							
Nonsmokers n[%(95%CI)]	221 [59.2 (54.9, 64.9)]	130 [51.2 (45.1, 57.3)]	0.046	<0.001	189 [73.3 (67.6, 78.3)]	56 [59.69 (49.6, 69.0)]	0.014
Exsmokers, n[%(95%CI)]	89 [23.9 (19.9, 28.5)]	50 [19.7 (15.3, 25.0)]	0.217	0.010	40 [15.5 (11.6, 20.4)]	15 [16.0 (9.9, 24.7)]	0.917
- duration yrs.	20.00 (13.50-30.00)	20.00 (10.00-25.00)	0.122	0.449	20.00 (10.00-30.00)	15.00 (7.00-20.00)	0.170
Current smokers n[%(95%CI)]	63 [16.9 (13.4-21.0)]	74 [29.1 (23.9-35.0)]	<0.001	0.048	29 [11.2 (7.9-15.6)]	23 [24.5 (16.9-34.0)]	0.002
- duration yrs.	30.00 (20.00-40.00)	27.00 (20.00-34.00)	0.039	0.423	30.00 (22.00-33.50)	28.00 (20.00-37.00)	0.462
- cigarettes/day	15 (10-20)	10 (10-20)	<0.001	0.041	10 (4-20)	20 (10-20)	0.001
Medication							
Antirheumatics NSADs[v] users n[%(95%CI)]	180 [48.3 (43.3, 53.4)]	133 [52.6 (46.5, 58.7)]	0.328	0.002	163 [63.2 (57.2, 98.9)]	69 [73.4 (63.7, 81.3)]	0.073
MTX[w] users, n[%(95%CI)]	180 [48.3 (43.3, 53.4)]	132 [52.0 (45.9, 58.1)]	0.362	ND	0	0	ND
Leflunomide users ,n[%(95%CI)]	59 [15.8 (12.5, 19.8)]	26 [10.3 (7.1, 14.6)]	0.048	ND	0	0	ND
Chloroquine users, n[%(95%CI)]	26 [10.2 (7.5, 13.7)]	33 [8.8 (5.9, 12.9)]	0.559	ND	0	0	ND
Sulphosalazine users, n[%(95%CI)]	96 [25.7 (21.5, 30.4)]	61 [24.1 (19.3, 29.7)]	0.659	Nd	0	0	ND

Glucocorticoide							
- users, n[%(95%CI)]	314 [84.2 (80.2, 87.6)]	213 [83.9 (78.9, 87.9)]	0.913	ND	0	0	ND
- duration (month)	4.0 (1.0-8.0)	2.0 (1.0-6.0)	0.008	ND	0	0	ND
- dose (mg/day)	20.0 (10.0-20.0)	20.0 (10.0-20.0)	0.632	ND	0	0	ND
Anti-TNF[y], n[%(95%CI)]	16 [4.3 (2.7, 6.9)]	24 [9.5 (6.5, 13.7)]	0.009	ND	0	0	0
Analg users, n[%(95%CI)]	134 [35.9 (31.2, 40.9)]	71 [28.0 (22.8, 33.8)]	0.037	0.945	92 [35.7 (30.1, 41.7)]	29 [30.9 (22.5, 40.3)]	0.401
Opioids users, n[%(95%CI)]	0	1 [0.4]	ND	ND	91 [35.3 (29.7, 41.3)]	30 [31.9 (23.3, 41.9)]	0.557
Antihypertensives							
ACE-I[x], n[%(95%CI)]	150 [40.2 (35.3, 45.8)]	0	ND	0.002	137 [53.1 (49.0, 59.1)]	0	ND
BB[z] , n[%(95%CI)]	113 [30.3 (25.9, 35.1)]	0	ND	0.930	79 [30.6 (25.3, 36.5)]	0	ND
DIUR[aa] , n[%(95%CI)]	121 [32.4 (27.9, 37.3)]	0	ND	0.004	113 [43.8 (37.9, 49.9)]	0	ND
ATRA[ab] , n[%(95%CI)]	13 [3.5 (2.1, 5.9)]	0	ND	0.173	15 [5.8 (3.5, 9.4)]	0	ND
CCB[ac], n[%(95%CI)]	94 [25.2 (21.1, 29.2)]	0	ND	0.001	96 [37.2 (31.5, 43.2)]	0	ND
Anti-HT[ad] , drugs. no	2 (1-2)	0	ND	0.008	2 (1-3)	0	ND
Anti-HT users, n[%(95%CI)]	280 [75.1 (70.5, 79.2)]	0	ND	0.002	222 [86.0 (81.2, 89.7)]	0	ND
Statins, n[%(95%CI)]	68 [18.2 (14.6, 22.0)]	17 [6.7 (4.2, 10.5)]	<0.001	0.003	75 [29.1 (23.9, 34.9)]	10 [10.6 (5.9, 18.4)]	0.001

Results are expressed as percentages and 95%CI, median values (interquartile range) or mean values (standard deviation) as appropriate.
[a]RA, rheumatoid arthritis; [b]OA, osteoarthritis; [c]HT, hypertenson; [d]NT, normotension; [e]CI, confidence interval, [f]BMI, body mass index; [g] ND, non-done, [h]W/H, waist/hip, [i]VASP, pain visual analog scale; [j]VASGH, General health visual analog scale; [k]HAQ, Health assessment questionnaire; [l]DAS28-CRP, Disease activity score, 28 joints and C-reactive protein; [m]DM, diabetes mellitus; [n]ESR, erythrocyte sedimentation rate; [o]CRP, C-reactive protein; [p]Chol, plasma cholesterol, [q]TG, plasma trigycerides, [r]HDL, high-density lipoprotein, [s]LDL, low-density lipoprotein; [t]Glc, plasma glucose; [u]RF, rheumatoid factor; [v]NSAIDs, non-steroidal anti-inflammatory drugs; [w]MTX, methotrexate, [y]TNF, tumor necrosis factor; [x]ACE-I, angiotensin-converting enzyme inhibitors; [z]BB, β-blockers; [aa]DIUR, diuretics; [ab]ATRA, angiotensin-II receptor antagonists; [ac]CCB**,** calcium channel blockers; [ad]Anti-HT, antihypertensives.

Comments to table 1-S

Comparison of HT and NT (normotensive) RA and OA patients

In both RA and OA patients, the HT subgroup was characterized by older patients and a higher proportion of the elderly, a longer duration of the disease (RA or OA), higher BMI and a greater proportion of overweight/obese patients, higher VASP, a higher proportion of dyslipidemic and DM patients and higher plasma LDL and triglyceride concentrations, compared with the NT patients. VASGH and HDL values were similar in HT and NT in both RA and OA patients.

The following variables had dissimilar differences between HT and NT patients in RA and OA: the proportion of female HT and NT patients was similar in the RA group, but higher in the HT patients of the OA group; WHR was higher in HT RA patients than in NT RA patients, but similar in HT and NT OA patients; ESR, CRP, Chol, LDL, and Glc concentrations were higher in HT than in NT patients in the RA group, but were similar in the HT and NT patients in the OA group. (Statistically significant difference for CRP in OA was so small that had no clinical significance).

Regarding variables measured only in the RA group, DAS28-CRP values and RF concentration were similar in the HT and NT patients, whereas HAQ was higher in the HT than in the NT patients.

Comparing HT and NT patients regarding smoking the HT group had a higher proportion of nonsmokers, a similar proportion of ex-smokers, and a lower proportion of current smokers than did the NT group for both RA and OA. The smoking duration of ex-smokers was similar in among the HT and NT patients with RA and with OA. For current smokers, the duration of smoking was similar and the number of cigarettes per day was higher in HT RA patients than in NT RA patients and lower in HT OA patients than in NT OA patients.

Regarding medications there were no statistically significant differences in the proportions of users of non-steroidal anti-inflammatory drugs (NSAIDs) between HT and NT patients in either the RA or OA group. The same was found for RA-specific medication, including various disease modifying anti-rheumatic drugs (DMARDs), glucocorticoids (GCs) and anti-tumor necrosis factor (anti-TNF) drugs. An exception to this finding was leflunomide, with a higher proportion of users in HT group and the use was associated with a higher prevalence of HT. than in nonusers (69.4 in users % vs. 58.1%, , P=0.048). Regarding GCs, only the duration of therapy was associated with HT; duration was longer in HT than in NT patients.

The proportions of antihypertensive users, in terms of their general use and in terms of specific drugs, were higher in OA HT patients than in the RA HT patients, except in the case β-

blockers and angiotensin-II receptor antagonists, which were used by similar proportions of patients in both groups.

Statins were used by a higher proportion of HT than NT patients in both the RA and OA groups, and the proportion of HT users was higher in OA than in RA patients.

Comparison of hypertensive RA and OA patients

The HT OA subgroup was characterized by higher age, a greater proportion of elderly patients, longer awareness of HT, higher BMI, a greater proportion of overweight/obese patients, a higher proportion of dyslipidemic and DM patients, and higher TG and Glc concentrations compared to HT RA patients. In contrast, the disease duration (RA or OA) was longer and ESR, CRP and LDL concentrations were higher in HT RA than in HT OA patients. The proportion of females, WHR, VASP, VASGH and Chol, HDL and creatinine concentrations were similar in HT RA and OA patients.

Table 2-S. Logistic regression analysis with HT[a] as dependent variable.

Variable	OR (95%CI)	P-value
RA[b] group (n=627)		
Age	1.063 (1.038-1.090)	<0.001
RA_duration	1.018 (0.985-1.053)	0.289
BMI[c]	1.108 (1.047-1.173)	<0.001
W/R[d] ratio	0.620 (0.042-9.193)	0.728
VASP[e]	1.006 (0.995-1.017)	0.304
HAQ[f]	0.972 (0.718-1.315)	0.853
Dyslipidemia	1.316 (0.805-2.1529	0.273
DM[g]	1.348 (0.445-4.090)	0.597
ESR[h]	1.008 (0.995-1.022)	0.217
Chol[i]	1.002 (0.921-1.089)	0.971
LDL[j]	1.047 (0.806-1.360)	0.732
TG[k]	1.206 (0.920-1.581)	0.174
Creatinine	1.014 (1.000-1.028)	0.042
Glc[l]	1.113 (0.874-1.418)	0.386
Cigarette per day	0.977 (0.943-1.013	0.212
Glucocorticoid . duration of therapy	1.036 (0.976-1.099)	0.246
OA[m] group (n=352)		
Age	1.052 (1.020-1.085)	0.001
OA duration	1.036 (0.994-1.079)	0.095
BMI[c]	1.126 (1.051-1.207)	0.001
VASP[d]	1.023 (1.009-1.037)	0.001
Dyslipidemia	1.818 (1.011-3.270)	0.046
DM[e]	1.606 (0.637-4.046)	0.315
TG[f]	1.223 (0.875-1.710)	0.239
Cigarettes per day	0.950 (0.890-1.014)	0.126

Variables significantly different between HT and NT subgroups (table 1-S) were introduced in the model. HT[a], hypertension; RA[b], rheumatoid arthritis; BMI[c] , body mass index; W/R[d] ,waist/hip; VASP[e],pain visual analog scale; HAQ[f], Health assessment questionnaire;DM[g] ,diabetes mellitus; ESR[h] erythrocyte sedimentation rate; Chol[i],plasma cholesterol;LDL[j] low-density lipoprotein, TG[k] plasma triglicerides; Glc[l] , plasma glucose, [m]OA, osteoarthritis,.